

Changes in the Hemostasis System During the Recovery Period of Children from COVID-19

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Abstract COVID-19 is an acute respiratory viral infection in children, accompanied by damage to the it can cause various forms of pneumonia, respiratory failure of varying degrees, septicemia and septic shock. In severe forms of the disease, inflammation of the blood vessels and changes in the hemostasis system can endanger the child's life or lead to a deterioration in the quality of life, disability.

Keywords COVID-19, Children, Hemostasis, Hypercoagulation, Disability

1. Introduction

Viral diseases account for 80% of infectious diseases, according to the World Health Organization (WHO). The appearance of new infectious diseases in the last 10 years and the development of severe autoimmune pathologies, an increase in the number of allergic patients, are leading to a change in the structure of diseases in childhood. Although the new coronavirus infection, which was registered in 2019, was milder in children than in adults, we observe a significant increase in the incidence among children in the following years, the length of the recovery period after an acute course of the disease and the negative impact on children's lives and quality of life with complications observed in various organs and systems [1]. The clinic of the disease manifests itself after 2-4 days after the infection of the virus. The disease is acute, begins with an increase in body malaise, signs of general poisoning, which are not clearly developed. Also, when breathing in children, chest pain, cough, dry whistling wheezes are heard. Coronavirus infection can be complicated by acute pneumonia. Radiographs of the chest reveal foci or interstitial infiltrates. In severe cases, the activity of the respiratory organs worsens, in the second week the disease develops respiratory symptoms, in adults there is a violation of the function of various organs. In severe forms of the disease, injuries to the lower parts of the respiratory tract are observed, symptoms of pneumonia, sepsis, septic shock appear and can cause the patient's death [3,8].

According to the recommendation of the staff of the British pediatric service, the causes of complications of coronavirus

in children:

- background diseases, i.e. anemia, endocrine diseases, chronic diseases, including various developmental defects, bronchopulmonary dysplasia);
- cases of immunodeficiency caused by various causes;
- coinfection with respiratory syncytial virus, influenza virus and other pathogens.

Complications of COVID-19 are more common in people with chronic non-infectious disease. The risk group includes people with bronchial asthma, diseases of the endocrine system, i.e. diabetes mellitus, nutritional disorders, as well as those taking a number of drugs: antibiotics, cytostatics, glucocorticoids [9]. Severe inflammation develops in the severe course of COVID-19 and disorders in the management of the immune system arise. The in a general blood test, the formed elements of the blood, such as monocytes and lymphocytes, are reduced. The ratio of types of T-lymphocytes is disrupted.

In some patients with a rapid course of the disease, a "cytokine storm" develops due to increased production of interleukins. That is, the body will not be able to regulate the inflammatory process. The body's immune cells are produced in large quantities and affect internal organs [6].

After exposure to coronavirus, tissues attract protective blood cells such as monocytes, lymphocytes, and neutrophils. In this process, Th1 and Th17 produce inflammatory and proinflammatory cytokines, as well as chemokines [8]. Thus vicious circle appears and, in addition to causing "cytokine storm", enhances its development, as well as a severe inflammatory process. This condition leads to multiple organ dysfunction syndrome and severe consequences [9,10]. A postmortem examination revealed a large number of CCR6+, Th17, and increased activity of cytotoxic T-lymphocytes (CD)⁺ and NK-lymphocytes (CD16)⁺ in the affected organs [11].

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An increase in the number of cytotoxic cells does not indicate their normal functioning. The developing lymphopenia is associated with fatigue of cytotoxic lymphocytes under the influence of coronavirus. Macrophages in the se can be damaged by SARS-CoV-2 and, in turn, lead to the development of lymphopenia.

Simultaneously, mononuclear cells in peripheral blood stimulate the production of IL6/II8, attract neutrophils to tissues, and induce an uncontrollable inflammatory response of the body [9]. According to the data presented in the literature, COVID-19 infection in children is more damaging to the nasal cavity, larynx in comparison with lung tissue.

The initial period of coronavirus is from two to fourteen days, on average, 5-7 days, and even during this period, patients transmit the disease to those around them, even after the complete disappearance of clinical signs of the disease, for 7-17 days the patient is dangerous for those around him, that is, the disease is contagious [12].

The purpose of the examination: to prevent complications

observed after COVID-19 and disability among children.

2. Examination Material and Methods

For the examination, 82 children were selected who had COVID-19 in severe form, were treated in Tashkent City, children's infectious Diseases Hospital No. 3.

3 months after leaving the hospital from children, clinical symptoms were collected on a survey basis and a clinical examination (skin color, skin dressing condition, muscle tone and trophic, active and passive movements in the joints, breathing and pulse number, arterial blood pressure) was carried out, as well as their laboratory indicators (general blood analysis, blood biochemical analysis, coagulogram) were examined.

3. Personal Examination

Table 1. Changes in hemostasis rates in children controlled during recovery (M±m)

Index	Healthy control group n=40	With hypercoagulation n=29	With hypocoagulation n=14	Reliability <P
Platelet count (x10 ⁹ / l)	281,3±11,3	362,1±7,7	110,2±3,8	<0,01
BCT, second	308,9±3,2	132,4±5,1	392,4±12,5	<0,001
BT, second	108,0±1,81	76,8±1,3	128,0±4,1	<0,001
PTT, second	33,9±1,8	22,6±0,62	42,4±1,4	<0,001
PTI, second	13,8±1,2	10,4±0,32	16,4±0,54	<0,05
PTI, %	90,93±1,15	148,6±3,2	70,4±2,5	<0,001
INR, unit	1,02±0,03	0,65±0,02	1,42±0,05	<0,001
TB, second	27,8±1,1	15,4±0,48	34,2±1,2	<0,001
Fibrinogen g/l	3,38±0,21	7,8±0,18	2,4±0,11	<0,001
SFMC, g/l	2,81±0,05	9,85±0,31	9,24±0,32	<0,001
D-dimer, mkg/ml	0,20±0,05	0,96±0,03	0,78±0,03	<0,001

Note: P(<0.05) is a statistically reliable difference and P(>0.05) is a statistically unreliable difference in indicators compared to a comparison group.

Table 2. Hemogram parameters of children in our observation (m±m)

Hemogram	Main group		Control group n=39
	With hypocoagulation n=29	With hypercoagulation n=14	
Erythrocytes, 10*12/l	3,3±0,02	3,6±0,01	4,4±0,01
Hemoglobin, g / l	93,5±1,08	105,0±1,97	112,0±1,97
Color indicator	0,8±0,02	0,90±0,02	0,93±0,02
Leukocytes, 10*9/l	8,51±0,19	7,42±0,25	5,93±0,25
branched neutrophils	0,11±0,06*	0,09±0,02	0,08±0,02
Segmented	3,31±0,41*	2,9±0,08	2,6±0,08
Lymphocytes	31,56±0,96	29,06±1,06	27,06±1,06
Monocytes	0,58±0,07*	0,40±0,02	0,36±0,02
Eosinophils	3,96±0,04	2,78±0,17	2,18±0,17
Platelets	330,1±7,7	253,06±3,43	231,3±11,3
ESR, mm / h	9,79±0,12	7,89±0,01	4,89±0,01

Note * - values are important for a group of somatically healthy children, p<0,05-0,001.

A comparative analysis of the indicators of the blood clotting system in controlled children during the recovery period made it possible to identify a number of changes in relation to healthy children, which in turn manifest themselves in the form of hypercoagulation and hypocoagulation. We isolated patients undergoing hypercoagulation and hypocoagulation changes in the hemostasis system.

According to a coagulogram analysis, 29 of the children in our observation (35.3%) had hypercoagulation, 14 (17.1%) had hypocoagulation, and 39 (47.5%) had no changes.

In a hemogram analysis of children with COVID-19 during recovery, a decrease in hemoglobin levels and a decrease in color index ($P < 0.001$) of patients in the main group were found to have negligible ECG acceleration (Table 2). This can be explained by the fact that children in this group have anemia from burning pathologies. In the main group of patients, the leukocyte formula recorded an increase in the total number of leukocytes ($P < 0.001$), monocytes ($P < 0.05$) and rod-shaped ($P < 0.01$) and segment-core neutrophils ($P < 0.05$) as well as eosinophils.

4. Conclusions

In children's practice, a special place is occupied by a violation of the hemostasis system, which occurs as a result of a violation of the balance of the body's internal environment as a result of the influence of various exogenous and endogenous factors.

Impaired hemostasis balance in the body of morphofunctionally immature children has a negative effect on their overall health. Deep changes observed in the hemostasis system of organism cause clinical manifestations of hemorrhagic syndrome.

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